Bright Minds Biosciences Announces Positive Topline Data for its First-in-Human Phase 1 Study of Lead Compound, BMB-101

-- BMB-101 is a highly selective and potent 5-HT_{2C} agonist being developed for the treatment of refractory epilepsies and other indications, such as psychosis, addiction, and impulse control disorders

-- BMB-101 demonstrated an excellent safety and tolerability profile in single ascending dose, multiple ascending dose and food effects study

-- BMB-101 demonstrated central target engagement and predictable plasma pharmacokinetics

VANCOUVER, British Columbia, July 20, 2023 -- Bright Minds Biosciences Inc. (CSE:DRUG) (NASDAQ:DRUG) ("**Bright Minds**" or the "**Company**"), a biotechnology company focused on developing novel drugs for the targeted treatment of neuropsychiatric disorders and refractory epilepsy, today announced the successful completion of its three-part Phase 1 study of BMB-101. The study, conducted in Adelaide, Australia, by CMAX Clinical Research, a clinical trial center specializing in a range of early-phase trials and first-in-human studies, evaluated the safety, tolerability, pharmacokinetic (PK), and food effect in healthy volunteers.

BMB-101 is a highly selective and potent 5-HT_{2C} agonist being developed for the treatment of refractory epilepsies and other indications, such as psychosis, addiction, and impulse control disorders. BMB-101 demonstrated an excellent safety and tolerability profile. 5-HT_{2C} target engagement was demonstrated by transient, dose-dependent increases in prolactin. BMB-101 exhibited predictable plasma pharmacokinetics with relatively small inter-individual variability. The current formulation allows for twice-a-day oral dosing, and with further formulation development, there may be potential for once-a-day dosing. Based on these observations, the Company believes that moderate doses of BMB-101 will fully engage 5-HT_{2C} receptors, and therefore not be dose-limited by side effects, which will help to achieve maximal efficacy in future Phase 2 studies. Dose limited side effects exhibited by first generation 5-HT_{2C} agonists have prevented exploiting the full potential of this pharmacological mechanism.

"We are highly encouraged by the Phase 1 study observations and results, which give us confidence in selecting doses of BMB-101 for testing in refractory epilepsies and other disorders where serotonin 2C agonists are indicated. Learnings from the study will inform our path forward as we seek to develop effective therapeutic options with convenient dosing regimens for patients," stated Mark A. Smith, M.D., Ph.D., Chief Medical Officer of Bright Minds.

"There is a great opportunity and an unmet need to develop improved treatments for these and potentially numerous other indications, including psychosis and addiction disorders. The successful and on-time completion of the study is an important achievement for us, as we continue to evolve from a drug discovery to a drug development stage company. BMB-101 is now a Phase 2 ready asset, and we look forward to sharing our further progress," stated Ian McDonald, CEO of Bright Minds.

The Company is currently awaiting the qEEG (Quantitative Electroencephalogram) data and will provide a more detailed discussion of the Phase 1 results when available.

About the Phase 1 Study

Part 1 – Single Ascending Dose

- 4 cohorts (6 drug and 2 placebo) – single dose (oral solution)
- Reached the planned top dose of 180 mg/70 kg, which approached preclinical exposure limits
- Well tolerated with predictable PK
- Most common adverse event was oral paresthesias from liquid formulation

Part 2 – Food Effect

- 12 subjects – crossover with and without breakfast, 120 mg/70kg
- Effect of food on BMB-101 levels was relatively small, and therefore BMB-101 can be administered without the need for fasting

Part 3 – Multiple Ascending Dose

- 4 cohorts (6 drug and 2 placebo) – twice a day dosing for seven days after meals
    - Reached a top dose of 150 mg/70 kg twice a day
- Biomarkers for central target engagement: Prolactin release and qEEG

Good Manufacturing Practices (GMP) production completed for BMB-101 drug substance and drug product.

About BMB-101

BMB-101, a highly selective 5-$HT_{2C,}$ Gq-protein biased agonist, has demonstrated compelling activity in a host of *in vitro* and *in vivo* nonclinical tests. Compared to Lorcaserin, BMB-101 exhibits strong Gq biased signaling, coupled with minimal beta-arrestin recruitment. Bright Minds believes that G-protein biased signaling translates to better tolerance profile for this second-generation 5-HT_{2C} agonist, making BMB-101 a best-in-class 5-HT_{2C} agonist. Mechanistically, Serotonin (5-Hydroxytryptamine, 5-HT) is a monoamine neurotransmitter widely expressed in the central nervous system, and drugs modulating 5-HT have made a major impact in mental health disorders. Central 5-HT systems have long been associated with the control of ingestive behaviors and the modulation of the behavioral effects of psychostimulants, opioids, alcohol, and nicotine. Results of clinical trials and animal studies indicate that 5-HT_{2C} receptor agonists may have therapeutic potential in the treatment of addiction by decreasing the intake of opioids as well as impulsive behavior that can escalate compulsive drug use. BMB-101 is a new chemical entity (NCE) and constitutes as a novel scaffold 5-HT_{2C} agonist.

5-HT_{2C} agonism is a well proven anticonvulsant mechanism. In translational animal models, BMB-101 demonstrated a significant reduction in both the number and intensity of epileptic seizures and is a promising candidate for the treatment of Dravet Syndrome and other epilepsies. The Phase 1 trial (NCT 05397041) has been completed and BMB-101 is now Phase 2 ready.

About Bright Minds

Bright Minds is focused on developing novel transformative treatments for neuropsychiatric disorders, epilepsy, and pain. Bright Minds has a portfolio of next-generation serotonin agonists designed to target neurocircuit abnormalities that are responsible for difficult to treat disorders such as resistant epilepsy, treatment resistant depression, PTSD, and pain. The Company leverages its world-class scientific and drug development expertise to bring forward the next generation of safe and efficacious drugs. Bright Minds' drugs have been designed to potentially retain the powerful therapeutic aspects of psychedelic and other serotonergic compounds, while minimizing the side effects, thereby creating superior drugs to first-generation compounds, such as psilocybin.

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This news release includes certain statements that may be deemed "forward-looking statements." All statements in this new release, other than statements of historical facts, that address events or developments that the Company expects to occur, are forward-looking statements. Forward-looking statements are statements that are not historical facts and are generally, but not always, identified by the words "expects," "plans," "anticipates," "believes," "intends," "estimates," "projects," "potential," and similar expressions, or that events or conditions "will," "would," "may," "could," or "should" occur. Forward-looking information in this news release includes statements related to plans for future formulation development including to achievement of once-a-day dosing in respect of BMB-101, the implementation of Phase 2 trials, and the Company completing its strategic transition from drug discovery to drug development. Although the Company believes the expectations expressed in such forward-looking statements are based on reasonable assumptions, such statements are not guarantees of future performance and actual results may differ materially from those in the forward-looking statements. Factors that could cause the actual results to differ materially from those in forward-looking statements include continued availability of capital and financing, results of Phase 2 clinical trials with respect to BMB-101 and other compounds that the Company may seek to test in the future, results of further development activities related to dosing and the findings specifically related to once-a-day dosing, regulatory conditions with respect to in-human drug trials, and general economic, market or business conditions. Investors are cautioned that any such statements are not guarantees of future performance and actual results or developments may differ materially from those projected in the forward-looking statements. Forward-looking statements are based on the beliefs, estimates and opinions of the Company's management on the date the statements are made. Except as required by applicable securities laws, the Company undertakes no obligation to update these forward-looking statements in the event that management's beliefs, estimates or opinions, or other factors, should change.